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SHOULD VITAMIN D BE GIVEN ONLY TO INFANTS?

VITAMIN D has been so successful in preventing rickets during infancy that there has been little emphasis on continuing its use after the second year.

But now a careful histologic study has been made which reveals a startlingly high incidence of rickets in children 2 to 14 years old. Follis, Jackson, Eliot, and Park* report that postmortem examination of 230 children of this age group showed the total prevalence of rickets to be 46.5%.

Rachitic changes were present as late as the fourteenth year, and the incidence was higher among children dying from acute disease than in those dying of chronic disease.

The authors conclude, "We doubt if slight degrees of rickets, such as we found in many of our children, interfere with health and development, but our studies as a whole afford reason to prolong administration of vitamin D to the age limit of our study, the fourteenth year, and especially indicate the necessity to suspect and to take the necessary measures to guard against rickets in sick children."

*R. H. Follis, D. Jackson, M. M. Eliot, and E. A. Park: Prevalence of rickets in children between two and fourteen years of age, Am. J. Dis. Child. 66:1-11, July 1943.

In Memoriam

TO PRESIDENT ROOSEVELT

"Within the hour of this Sunday Morning Conference all that was mortal of a great and beloved leader has been laid to rest on the shores of the Hudson amid the peaceful hills of the valley he loved so well.

"It is fitting that we pay tribute to the strong and courageous spirit of one who experienced himself an affliction peculiar to childhood whereby his interest and sympathy were especially enlisted in the cause of handicapped children and as a result of which untold benefit has been bestowed upon thousands of young lives, not only through the material benefits of rehabilitation, but through the encouragement of unexampled precept and bravery of spirit.

"To the memory of a colleague equally interested in the healing of the afflicted, a large part of whose life work was devoted to interests identical with our own, we would dedicate this moment of silence in grateful appreciation."

SPECIAL REPORT

SYMPOSIUM ON PATENT DUCTUS ARTERIOSUS*

Dr. Bernard Walsh†

The ductus arteriosus is a structure necessary for intrauterine development. However, with very rare exceptions it is unnecessary after birth. Functionally it closes in almost every child after birth, although anatomically it remains patent for two to three weeks. I say functionally because if there were significant patency then we would have some evidence of it in newborns. When there is coarctation of the aorta or severe pulmonary stenosis, the patent ductus acts as a compensatory phenomenon and is necessary sometimes for the continuation of life. Otherwise a patent ductus arteriosus is a handicap.

The ductus arteriosus is a fistulous opening from 6 to 10 mm. in length. It varies in diameter from 3 or 4 mm. to 1 cm. It runs from the base of the left pulmonary artery to the arch of the aorta. When the duct remains patent after birth the shunt of blood is from the aorta to the pulmonary artery because the pressure is less in the pulmonary artery. It has been shown in experimental animals and in humans that as much as 75% of the blood from the left ventricle will escape from the aorta to the pulmonary artery in patients with patent ductus arteriosus. The blood that escapes is thrown right back into the lungs and to the left side of the heart, and the left side of the heart therefore undergoes strain and eventual hypertrophy in patients with patency of the duct. So, although a patent ductus arteriosus is considered a congenial cardiac defect, it really is a congenital vascular defect—an arteriovenous fistula.

Kennedy has shown by using pig embryos kept under water that the ductus could be closed whenever oxygen was introduced into the venous system or into the umbilical veins.[1] Therefore it is conceivable that a patent ductus arteriosus may be an acquired defect due to some interference with the blood supply immediately after birth.

In 7,500 consecutive routine autopsies at the Massachusetts General Hospital, there were found only 5 instances of patent ductus arteriosus.[2] Patent ductus arteriosus is about the third most common type of congenital cardiac disease that we see clinically. Two-thirds of the reported cases of patency of the ductus have been in women. Why there is this preponderance of occurrence in females is not known.

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* Presented at the Clinical Conference, March 5th, 1945.

I think there is only one practical way to make a diagnosis of patency of the ductus arteriosus, and that is on the basis of the finding of a continuous murmur with systolic accentuation maximal in the 2nd left interspace. If this particular murmur is not present then a patent ductus does not need serious consideration. However, there are a few reliable reports of patients with patent ducts either at autopsy or at operation who during life had only a systolic murmur. I have seen here one patient with only a systolic murmur along the upper left sternal border, who a year later had the characteristic continuous murmur with systolic accentuation. Also there have been reported one or two patients who did not have any murmur. There are other characteristic physical phenomena in some of these patients with patent ductus arteriosus, namely low diastolic blood pressure, and occasionally an additional diastolic rumbling murmur at the apex. The latter is due, I believe, to ventricular dilatation. The first patient operated by Dr. Gross in Boston had this murmur which disappeared after operation.

The electrocardiograms are normal with few exceptions, those being mostly in patients who have very large left ventricles as a result of the strain caused by a widely patent duct.

I do not think the x-ray is of any assistance in making the diagnosis. The most important information we get from x-ray concerns heart size and the consequent evidence concerning the probable diameter of the duct and as to the urgency of the need for operation. Most of the patients that I have seen who have had patent ducts have not had any particular prominence of the pulmonary artery by fluoroscopy or x-ray in the posterior-anterior view, and sometimes even in the oblique views. The so-called hilar dance frequently mentioned in the literature as a characteristic in these patients has been absent in many of our cases. On the other hand, a readily noted hilar dance is not uncommon in slender, excited patients who have slight elevation of the systolic blood pressure and who have no heart or vascular disease.

Patients with patent ductus arteriosus appear to be well as a rule. When the defect is not complicated there is no cyanosis, and when there is a complicated lesion the patients usually die before the age of one year.

Concerning prognosis in patency of the ductus arteriosus we have no exact knowledge. Only autopsy data are found in the literature, and on the basis of that, the outlook is bad. From several series reported one would conclude that 70% of all patients who live beyond the first year will expire before they reach 40 years of age. Or, in another manner of speaking, the expectancy of life for those reaching

17 years with patent ductus arteriosus is shortened by some 23 years in men and by 25 to 28 years in women. We infrequently see patients with patent ductus arteriosus over 30 years of age. We do see them in their teens, but then they seem to disappear. However, I know of two living persons with patent ductus arteriosus who are over 60 years of age.

Of the patients who have died and who have been reported, about 40 per cent died of heart failure, 30% of subacute bacterial endarteritis, and 3% of rupture of the duct.

As long ago as 1907 Munro published a paper suggesting slitting the sternum and getting at the ductus arteriosus.[3] However, it was not until 1937 that ligation was first attempted. The first operation was done by Strieder on a patient with bacterial endarteritis.[4] The operation was not successful, and at autopsy the duct was found to be a fistula which could not have been ligated. Then Dr. John Hubbard urged Dr. Gross (both of Children's Hospital, Boston, Mass.) to operate on patients with ductus arteriosus. In 1938 at Children's Hospital in Boston the first successful ligation was done by Dr. Robert Gross on a girl with a very large heart who would have died of heart failure before many years.[5] Since then perhaps three or four hundred ligations have been carried out in this country with remarkable success. In November 1944 Gross reported a total of 54 operations in the last 14 of which he had severed the ductus. He suggested first in 1938 that severance was probably feasible, and that it would be important to do this operation for patients with infected ductus. Dr. Touroff of New York City[6] was the first actually to sever the ductus, and also the first to ligate the ductus in patients with subacute bacterial endocarditis. About 14 per cent of the patients operated by Dr. Gross in the early months of his experience had a return of the murmur, and for this reason he developed the daring technique of severing the duct to its present very successful state.[7]

The total mortality from the operation has been about 10%. In the series of cases here there hasn't been any mortality. The greatest difficulties encountered in the operation concern the freeing of the posterior margins of the duct without tearing the structure.

There are certain reasons why a patient should not have the operation. The chief objection would be the presence of other complicating congenital cardiac defects. However, even when there are complicating congenital defects, the procedure might be carried out, particularly in patients who have also subacute bacterial endocarditis or endarteritis, for the surgeon could pinch the duct to estimate the effect

of the ligation. However, with the advent of penicillin and the recent favorable reports of its effect in subacute bacterial endocarditis, operation may not always be considered important for these patients. Other reasons for not attempting ligation would be very severe persistent heart failure and serious extra cardiac disease.

The specific results reported here concern nine patients with patency of the ductus, upon whom ten operations were done. There have been complete cures in seven. There has been a qualified cure in one, and one boy has had recanalization despite two operations. Only one of our patients, a girl of 22 years, had subacute bacterial endarteritis. This patient left the hospital apparently cured of both her patent ductus and her infection. She died at home about six weeks after leaving the hospital, apparently of severe gastric hemorrhage induced by heparin. She did not feel well about a month after she went home, and consulted her family physician who suspected a recurrence of her bacterial infection. One blood culture was positive for streptococcus viridans. After

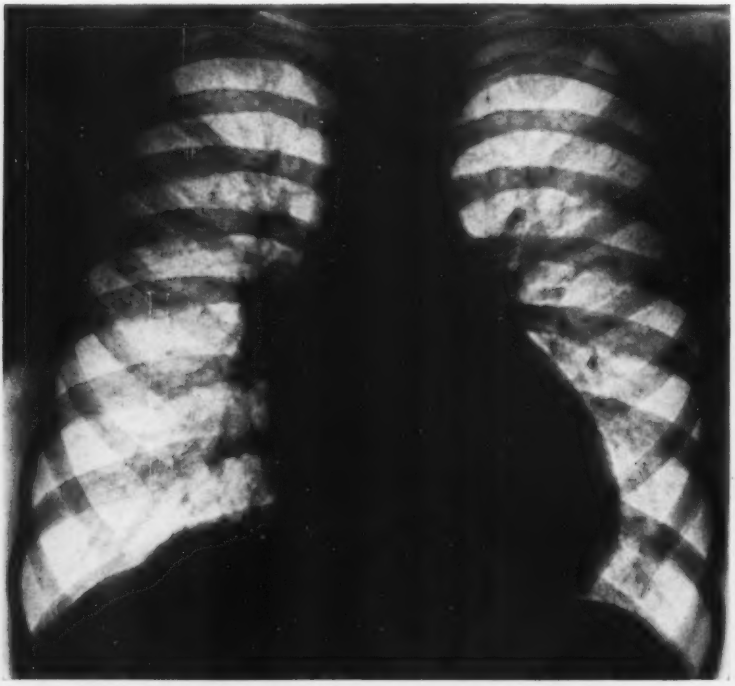

FIG. 1. E. S. NOTE THE APPARENTLY NORMAL CONTOUR OF THE HEART IN THIS CASE OF PATENT DUCTUS ARTERIOSUS.

a few days of treatment with sulfadiazine and heparin, she vomited a large amount of blood and died shortly thereafter. No autopsy was done. It is not clear exactly what happened to this patient, although we are certain from the physician's description that there was no return of the murmur characteristic of patency of the ductus arteriosus. One patient, a boy 17 years of age, had the operation done twice. After the first operation the duct was obviously still patent, possibly due, Dr. Davis thought, to slipping of one of the ligatures. Two and one half weeks after the first operation Dr. Davis again ligated the duct. The patient got along well and the murmur was absent but only for six weeks. At the present time the murmur is about 50 per cent less loud than before the first operation. Just why this patient was not cured by operation as were the others in our series we do not know. We assume that the ductus has recanalized. This patient is otherwise well able to carry on normal activity.

The first patient operated on by Dr. Edgar Davis was a five-year-old

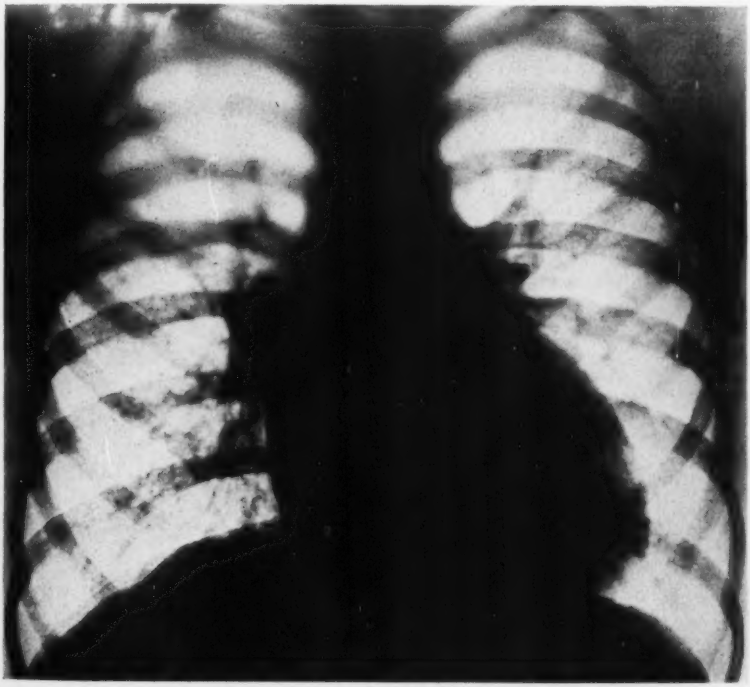

FIG. 2. E. S. AFTER ONE YEAR'S OBSERVATION, THE HEART HAS SIGNIFICANTLY ENLARGED.

girl from our Cardiac Clinic here with a very large heart. She has been entirely well and her heart has gradually decreased in size so that it is now within normal limits. This result has been duplicated in the other young patients whose hearts were particularly large before operation. Our most recent patient, a 44-year-old woman, has done very well. There has been no evidence postoperatively of patency of the ductus but her heart has not decreased in size. I suspect her heart will continue to be large, decreasing little if any, since at her age the enlargement is probably due to hypertrophy with little dilatation.

Examination of the cured patients is in striking contrast to their pre-operative examination. The characteristic murmur has disappeared, the heart has become quiet, the diastolic blood pressure if it was low preoperatively is now well within normal limits and in a few patients for a short time there has even been a slightly higher diastolic level than the average normal. The systolic blood pressure either has decreased slightly or has remained unchanged.

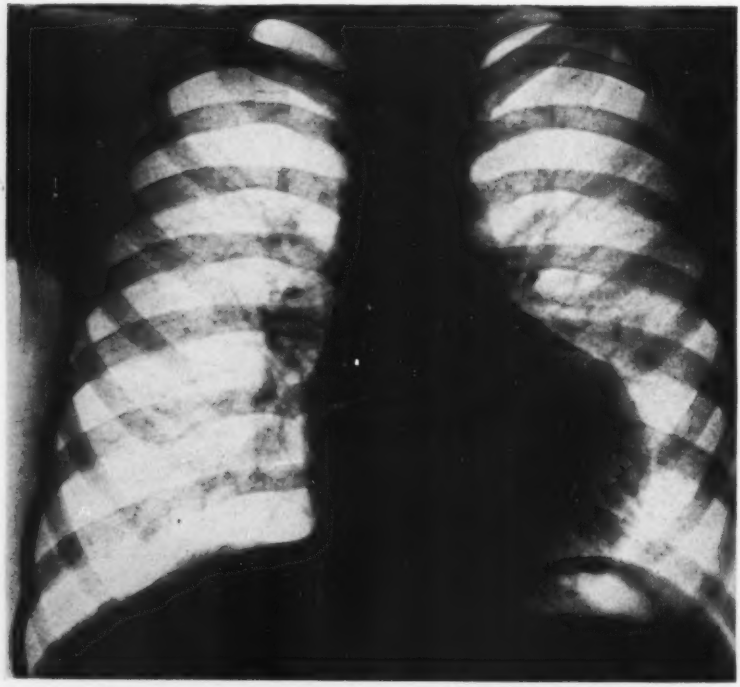

FIG. 3. E. S. ONE MONTH AFTER LIGATION OF PATENT DUCTUS. NOTE THE STRIKING CHANGE IN THE CONTOUR OF HEART

It is my opinion and Dr. Davis' that all patients with patency of the ductus arteriosus should be operated upon since the dangers of not being operated on seem to far outweigh the risk of the operation. We are sure that the operation should be urged for those who have large hearts or whose hearts have been getting larger under observation, who have heart failure, or who have subacute bacterial endarteritis. A good argument favoring operation is that a patent ductus arteriosus constitutes an economic handicap, for these patients are commonly rejected for employment. With successful ligation this objection on the part of the employers is often removed.

Dr. Edgar Davis:** I greatly appreciate the invitation to participate in this discussion this morning and permit me to openly commend and congratulate Dr. Walsh from two standpoints, first for his complete cooperation with the surgical service and secondly for his accuracy in diagnosis. We have not one time proven him to be wrong.

It has now been 8 years since my old co-worker, Dr. Strieder, from the University of Michigan attempted the first ligation of a patent ductus arteriosus. It being the first attempt, he was not quite so familiar with the anatomical structures as we are now and the operation was unsuccessful. Dr. Gross performed the first successful ligation. Our observations are based upon a series of 9 cases operated upon here and one case operated upon in another city.

When we first started doing these operations it behooved us to find out what happened to these cases if they were not treated. Assuming that the outcome justified the surgical proceedure then what kind of surgical result could be hoped for? We limited our first operations only to those cases in whom there was an absolute indication for surgery. At the same time, we felt that surgery was definitely indicated in the event that there was low diastolic pressure or a patient less than 17 years old with a diastolic blood pressure less than 50. There was quite a bit in the literature concerning the physical and mental development in these children. I don't attach any significance to them. Our undersized patients are still undersized and their growth in stature has not materially increased after ligation of the patent ductus has been performed. Sub-acute bacterial endarteritis, we believe, is always a definite indication regardless of age.

From a surgical standpoint we have used four different surgical approaches. On our first case, we used the original technique described by Gross who went through the second interspace and transected the second and third cartilages. He operated on a little baby 20 months

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old and was amazed at the difficulty in identification of anatomical structures. On the next case we used a lateral approach. We used that type of incision on a couple of cases and found it went fairly well. Then we started using the posterior approach and did four cases that way. A large segment of the fourth rib and shorter segments of the third and fifth ribs were taken out providing excellent exposure, but anatomically in attempting to separate the duct we found that we were working over the arch of aorta which caused some difficulty. Since then we have used an incision starting from the second cartilage and carried downward and back to the posterior axillary line; the third intercostal muscle can then be split which permits the insertion of a pair of rib spreaders thus opening up the entire thorax. In a woman this is particularly desirable because the incision is made below the breast leaving no visible scar. When the thorax is opened here, you find a very enlarged pulmonary artery. It is so large that it almost completely obstructs the arch of the aorta. The anesthetist can tell what the surgeon is doing by two things. When one puts a finger on the ductus and presses it, the heart rate slows down to 90 or 100 or even less and at the same time the diastolic pressure immediately becomes elevated. We used to think that a low diastolic pressure was a definite indication for surgery but now it is not regarded as of tremendous clinical significance.

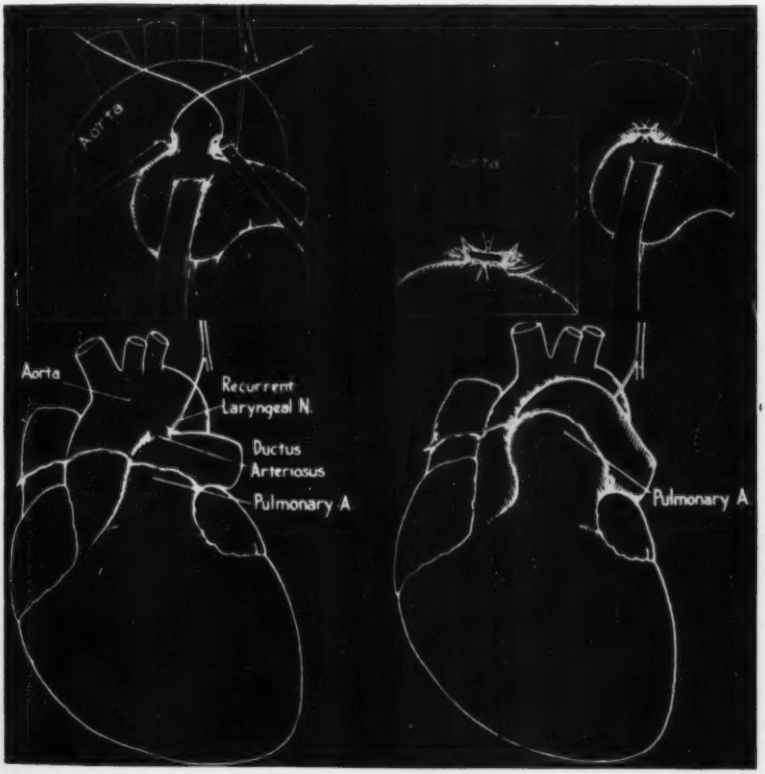
I have never used any suture material for these ligations, utilizing the experience of others who have had fatalities. Instead, I have used No. 7 umbilical tape in my cases.

Dr. Edward Lewis: I would like to ask if Dr. Walsh and Dr. Davis are going to extend surgical intervention to those children of the younger age group, namely under 5 years of age, in whom the mortality is so high?

Dr. Davis: I don't think so. For example, right now we do not know what percentage of these patent ducts co-exist with other anatomical defects. I was quite interested in Dr. Walsh's remark in which he stated that we should reserve surgery for patients 5 years or over since better results are obtained in the age group from 5 - 12 years. I would not be adverse to doing surgery on an uncomplicated 4-year-old child if it was a moderately well developed patient. However when you start in on these very young children, it is difficult to identify your anatomical structures and besides the majority of them are associated with co-existing anomalies. If a child survives to 4 or 5 years of age the chances are more remote that he has some other co-existing anomaly.

Considering the fact that in patent ductus one may have an anatomical structure which is of larger diameter that it is long, it requires consummate surgical skill and courage to divide the duct after ligation as Gross has recently been doing. If and when we find a moderately long duct we will ligate it, divide it and sew it up. However I am not convinced in my own mind that it is absolutely necessary to divide it. I think our failures in some of our first cases were due to the fact that we used silk ligatures.

Dr. Costenbader: The recent opthalmic and pediatric literature have contained several reports noting the association of German measles during the first trimester of pregnancy with congenital eye and heart defects in the infant. It is of interest to know there is an infant in the hospital at the present time with microcephaly, bilateral congenital cataracts and a patent ductus arteriosus—the history of German measles in



the mother while she was pregnant, however, is at best doubtful. It is possible that infection during pregnancy, especially during the first trimester may profoundly influence genetic mutations and give rise to various abnormalities in the infant. Certainly the association would be worthy of further investigation.

Dr. Rice: It might be of some interest to know that at Children's Hospital we have listed in the necropsy files a total of 43 patients who had a patent ductus arteriosus which could be definitely stated to have contributed to the impairment of cardiac efficiency. This was during a period extending from 1932 up to the present time. Of this group 19 were representative of the relatively benign combination of patent ductus and foramen ovale; the remainder had other abnormalities of the heart, great vessels or other organs. Very few persons with patent ductus grow to their teens or adult life.

The diagnoses that come down to us in the Pathology Department on these children have been most encouraging. Very often now a diagnosis of patent duct is made whereas previously it was customary to list it only as a congenital anomaly without further elaboration.

It should be noted that, during post mortem examination, it is rather difficult to get at a structure such as a patent ductus. As can well be inferred, it requires considerable skill and experience on the part of a surgeon to approach and ligate this anomaly.

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ACUTE BENIGN EPIDEMIC LYMPHOCYTOSIS

Case Report No. 15

Dr. Mary Warner A.T.-41-87

A. T., a five-year-old colored female, was admitted to the hospital on the evening of January 1, 1945 with the chief complaints of abdominal pain and vomiting for one day. The pain was experienced the day before on December 31, 1944 and was generalized at the onset and later became localized in the right lower quadrant. Her father gave her one teaspoonful of castor oil in the afternoon and a similar dose in the evening. No relief was obtained. The girl was listless and refused to eat. On the morning of January 1, 1945 she began to vomit and continued to do so throughout the day. The abdominal pain had disappeared. She passed one watery stool just prior to admission but until this motion, the bowel movements had been normal. There were no previous similar attacks. The past history was essentially negative and the family, consisting of the parents and three siblings were apparently in good health.

The physical examination upon admission revealed a well developed, fairly well nourished colored girl of five years who was drowsy and showed evidence of a moderate dehydration. The temperature was 100°. The only positive findings in addition to the appearance of drowsiness and dehydration were injected tonsils and pharynx, several palpable, discrete but not enlarged cervical lymph nodes and slight tenderness on deep palpation of the abdomen, particularly on the right side. The liver and spleen were not palpable and no abdominal masses were felt. The impression on admission was acute gastritis or mild acute appendicitis. A stat white-cell count was done to aid in the diagnosis of appendicitis and the result was entirely unexpected. The leucocytes numbered 73,700 with 80% mature lymphocytes, and 17% neutrophils and 2% eosinophils. This count immediately raised the possibility of a blood dyscrasia. The absence of an enlarged spleen or liver, no lymph node enlargement, and lack of any evidence of anemia now were significantly negative findings. Added to the diagnostic possibilities were acute benign epidemic lymphocytosis and infectious mononucleosis.

Dehydration was combated with intravenous fluids on admission and on the morning of January 2, 1945 the vomiting had ceased. Her temperature was 99°. She was less drowsy but refused to eat. Supportive therapy was instituted. More extensive laboratory investigations

were carried out to determine the nature of the lymphocytosis and the following tests done in the course of the next two weeks were negative: blood Wassermann, spinal fluid examination, blood culture, heterophile agglutination tests (3), repeated urinalyses, stool examination for ova and parasites and the intradermal tests for trichinosis. The last two tests were indicated when subsequent blood counts revealed a persistent eosinophilia. Bone marrow smear showed no abnormalities and the thrombocytes of the blood were present in normal numbers. The results of the repeated blood counts are summarized in the table.

The hospital course was quite benign. She was drowsy for the first 2 - 3 days and then was more alert. On the 7th day she was playful and her appetite improved. There was a low grade fever which reached a peak of 102° on the 8th day and slowly fell to normal on the 15th day.

Hemograms were done on the members of the patient's family and a six-year-old sister had a leucocytosis of 25,000 cells with 60% lymphocytes. This child had an enlarged right cervical lymph node. She had no complaints.

The patient was discharged on January 15, 1945 and was to report to the Out Patient Department for weekly blood counts. However, three days after discharge, on January 18, 1945, she returned with a fever of 104.5° and appeared quite toxic. This time she presented a

Date	1-1-45	1-4-45	1-10-45	1-11-45	1-14-45	1-16-45	1-18-45
H B (gms)	11	12	10	9.5	11	9	10
R B C			3,970,000	3,640,000	3,540,000		
W B C	73,700	53,900	57,600	53,200	47,300	41,800	39,200
Neutrophils	17%	8%	9%	17%	23%	25%	18%
Eosinophils	2	4	3	5	10	7	19
Lymphocytes	80	77	80	71	64	64	60
Prelymphocytes			3				
Lymphoblasts			1			1	
Basophiles				2			2
Monocytes	1	11	4	5	3	3	1

definite cause for the fever. Her tonsils were enlarged, fiery red and studded with follicular abscesses. This acute follicular tonsillitis was believed to be coincidental with the lymphocytosis and not part of the

original illness. Her blood count interestingly enough at the peak of this toxic infection showed a leucocyte count of 39,200 and an eosinophilia of 19%. It is to be noted that as the total white count decreased the eosinophils increased in number. The throat infection resolved in two days after a short course of chemotherapy and the child was discharged four days later, completely well.

DISCUSSION

Dr. Frederic Burke: Benign infectious lymphocytosis is a rather rare condition in which there is a total increase in the number of leucocytes with a high proportion of lymphocytes and a lack of any other significant clinical manifestations. Only five reports on this condition have appeared in the literature and all of these with one exception have been noted since 1941.[1] Ryersbach and Levert[2] in their account of sixteen cases in February, 1941, found only one previously reported instance. It is probable that patients with this aberrant blood picture have been classified as having infectious mononucleosis despite the lack of confirmatory clinical findings or determinations of a high titre of heterophile antibodies in the blood.

The diagnosis is made by the demonstration of leucocytosis with a marked lymphocytic predominance. White-cell counts over 100,000 with 70-90% lymphocytes are not unusual in this condition. There is a lack of any significant systemic manifestations. The Paul-Bunnell test is negative. Lymphadenopathy may or may not be present. The infectious nature is evidenced in this case by the demonstration of a similar blood picture in a sibling. Finucane and Philips[1] recently reported an epidemic of twenty-one cases in the children's wards of an institution; their attempts to identify an etiologic agent were unsuccessful.

The differential diagnosis consists primarily in ruling out leukemia, infectious mononucleosis and whooping cough. Lymphatic leukemia is excluded by the benign course, normal platelet count and the lack of any significant signs. Infectious mononuclesois is usually accompanied by malaise, fever, lymphadenopathy, myalgia, splenomegaly, and a positive Paul-Bunnell heterophile antibody titre of 1:112 or higher. Although pertussis may have a similar blood picture, the clinical manifestations are usually sufficiently characteristic to rule it out.

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TYPHOID FEVER

Case No. 16

Dr. Alfredo Ceballos D.A. - 43-8797

D. A., a 12-year-old white boy, was admitted to the hospital on May 1, 1944, with the chief complaints of fever for eight days and abdominal pain for four days.

He had a previous admission in December, 1943, at which time he presented cardiac enlargement and a loud apical systolic murmur. The diagnosis of acute rheumatic fever with rheumatic heart disease was made. He was transferred on January 5, 1944 to the Christ Child Farm where his convalescence progressed uneventfully until 9 days before this present admission when he developed a fever of 103° and became weak and anorexic. He complained of headache and sore throat. For one week the temperature fluctuated between 103° and 104° and during this time he had two episodes of epistaxis. Shortly before entry he became delirious and drowsy and was transferred to this hospital with the diagnosis of an exacerbation of acute rheumatic fever.

Upon admission, physical examination revealed a well nourished, acutely ill, drowsy 12-year-old white boy who appeared to be in no respiratory distress. The temperature was 104°, pulse rate 120, respirations 40, blood pressure was 130/50. The tongue was dry and coated and a moderate pharyngitis was noted. A few scattered moist rales were heard over both lung fields. The heart was not enlarged to percussion, but a harsh, loud systolic murmur was audible at the apex with transmission to the left axillary region. The rhythm was regular. The abdomen was distended and tympanitic with some tenderness in the right lower quadrant. Liver and spleen were not palpable and no abdominal masses were noted. Skin was hot, dry and no rash was present. There was no lymph node enlargement. Neurological examination was essentially negative.

Hemogram showed a red-cell count of 3,870,000 and 10.5 gms. of Hgb. The white-cell count was 6,400 with 49% neutrophils, 46% lymphocytes and 5% monocytes. Urinalysis revealed 100 mgm. of albumin, 4 plus acetone and many white blood cells. Sedimentation rate was 29 mm. per hour.

On the 3rd day in the hospital, the clinical picture of typhoid fever seemed rather apparent. There was relative bradycardia, stupor, and

a dry furrowed tongue. The temperature had ranged consistently in the vicinity of 104°. The abdomen was distended, and although the spleen was not palpable there was tenderness upon moderate pressure in the left upper quadrant. Many macular "rose spots", which faded on pressure, appeared on the abdomen and back. Widal tests were performed, and eleven days after onset of the illness, the agglutination for Eberthella typhosa "O" was found to be positive in dilutions ranging between 1:20 to 1:640 and for antigen "H" from 1:20 to 1:320. The blood and urine cultures were negative for typhoid organisms. A stool culture obtained on the 19th day of the illness was positive.

The evolution of the disease was uneventful. The temperature remained at a high plateau for 14 days, oscillated for 3 days and then fell by lysis during the following week, reaching a normal level 29 days after the onset of the illness. Leucopenia persisted until the temperature returned to normal. The albumin disappeared from the urine on the 5th hospital day. No untoward complications occurred and the patient's cardiac lesion was not aggravated by the infectious process. It is worthy of note that successive crops of "rose spots" appeared in this patient over a period of two weeks, which is unusual.

Treatment was essentially supportive and symptomatic. Fluids and whole blood were administered intravenously. A high caloric, low residue, soft diet containing about 70 gm. of protein was given together with 200 mgm. of ascorbic acid daily. Reticulogen was injected daily in an attempt to stimulate production of red blood cells. The patient was discharged on the 54th hospital day after 2 successive urine and stool cultures were negative.

DISCUSSION

An interesting feature of this case was the discovery of the source of infection. The boy came from a convalescent home where the chances of contact are minimized by the strict hygienic measures that are employed there. An investigation conducted by the Health Department disclosed the source of infection. One of the nurses who had been taking care of the patient had had typhoid fever a few years before and was found to be a "typhoid carrier."

In this case the diagnosis of typhoid fever was entertained from the history and clinical picture before any confirmatory laboratory tests had been performed. The symptoms and signs were strikingly typical

of the disease. This infection is prevalent in rural sections where adequate laboratory facilities are scarce and physicians must depend principally upon the clinical picture to make the diagnosis.

A review of 35 cases of typhoid fever at this hospital from 1939 to 1944 revealed that the majority of cases occurred in children between the ages of 2 and 8 years with 2 cases under one year of age. The sources of contact were discovered in 60% of them. The peak incidence occurred in the summer and fall. Characteristic symptomatology was present in well over 50% of this series. A breakdown of this figure revealed anorexia in 85%, headache in 60%, abdominal pain in 40% and in 3% epistaxis. Physical findings were quite in accord with those usually found in children afflicted with the disease. The temperature charts showed a relatively high plateau for the first 10 days with a gradual defervescence and essentially normal temperatures during the following 10 days. Tenderness and abdominal distention was observed in about 50%. The spleen was enlarged in 20%, slightly below the average incidence. A typical macular rash was seen in 17% of the patients, all of these being white children. Blood cultures were positive in 50% of the cases, a few of which were taken after the 1st week of illness. Stool cultures were positive in 60% of the cases. Positive Widal agglutinations were present in 91% of the patients. Leucopenia with relative lymphocytosis was noted in 57%.

In all cases treatment was symptomatic and supportive. The average hospital stay was 28 days. In 4 cases, a complication of bronchopneumonia occurred. There was no mortality in this series, indicating a relatively good prognosis in children providing there is early recognition and early supportive treatment.

Large doses of ascorbic acid have been recommended for the treatment of typhoid fever, it having been demonstrated that the antibody level in the blood stream parallels the level of ascorbic acid in the blood. Hodgson [1] recommends the early use of "Vi" and "O" antisera in the severe cases; stating that the "O" combats the endotoxin. Streptothricin has not proved very satisfactory against typhoid fever.[2] In several South American countries, Bacteriophage is being used extensively, and claims have been made for its efficacy. Results obtained with such therapy in this country however have not been so encouraging.

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PAROXYSMAL HEMOGLOBINURIA

Case No. 17

Dr. Albert Orlosky E.F. - 45-455

This is a case of a three-year-old white male child who was admitted to Children's Hospital on January 11, 1945 because of the passage of dark urine. According to the mother the child had been perfectly well and active until this present illness. Six days prior to admission, the child fell on the sidewalk following which he began to complain of pain in his abdomen. Two days before admission the mother noticed for the first time that his urine was dark brown in color. He was kept in bed for the next two days and the urine cleared. On the day of admission he again passed dark, reddish urine and it was noted at this time that "his eyes were slightly yellow."

The patient had been a normal full term infant, delivered by a general practitioner, who stated that the mother had a negative blood Wassermann at that time. There were no previous illnesses except for two mild attacks of tonsillitis and a second degree burn about one year ago which healed without scarring. There was no hereditary illness or blood dyscrasias in the family history. A point of interest was the father's statement that he, himself, had been anemic all his life.

Positive physical findings upon admission were pallor, mild icterus of the sclerae, cervical and inguinal adenopathy, and a soft systolic murmur heard along the left border of the heart, loudest in the third interspace.

Daily urinalyses collected during the first five days were entirely negative. The hemogram revealed a red cell count of 2,000,000 with 7 gms. Hgb. The white cell count was 11,000 with 54% polys, and the platelet count was 60,000. Intravenous pyelogram was negative. X-rays of the skull and long bones did not reveal any abnormal changes. Other laboratory tests included a fragility test, non-protein nitrogen, sedimentation rate, bleeding and clotting times and total proteins all of which were within normal limits. Blood smears for malarial parasites were negative. The icterus index upon admission was 19 units. Van den Bergh reaction was indirect and the quantitative bilirubin content was 3.7 mgm. percent. These tests pointed to a hemolytic process but the nature of this was as yet undetermined.

Because of the anemia the child was given several blood transfusions. Following each transfusion, he had a reaction manifested by chills and fever. After the first reaction the child voided dark red urine which contained 500 mgm. percent of albumin and microscopically showed hyaline casts and disintegrated red-cells. The benzidine test was positive for occult blood. Urine specimens were again negative after forty-eight hours but showed a similar reaction after the third transfusion.

Upon closer questioning of the mother, it was learned that prior to both episodes of passing red urine before admission, the child had been out for a walk and had become severely chilled on both occasions.

The diagnosis of paroxysmal hemoglobinuria was confirmed by the Donath-Landsteiner test which demonstrated the presence of auto-isohemolysins. This test was also done on the father's blood and found to be positive. Cold agglutinins were also present in the child's blood. The blood Kahns of both parents and patient were negative. Because of the presence of cold agglutinins, another transfusion was given using warm fresh blood but the urine, negative before transfusion, was again dark red following the infusion.

DISCUSSION

Dr. Linson: Hemoglobinuria is a condition in which the blood pigments appear in the urine giving it a dark red to black color although only a few or no red cells may be present. The urine, in addition, contains a small amount of albumin, yields a positive benzidine test and shows the presence of hemoglobin or methemoglobin spectroscopically. The condition may be associated with various diseases such as scarlet fever, erysipelas, typhoid fever, malaria or it may follow incorrectly matched blood transfusions or result from poisoning by certain chemicals such as potassium chlorate or the sulfonamides. Severe burns may also cause hemoglobinuria. There has also been described an epidemic hemoglobinuria, so called Winckle's disease, which is characterized by hemoglobinuria, icterus, cyanosis and usually results in death.

Paroxysmal hemoglobinuria differs from the other types in that in the majority of cases it follows exposure to cold. This type rarely occurs in childhood and in 95 - 99% of the cases reported, syphilis has been diagnosed as the causative disease. However, in our case, there were no stigmata of syphilis and the serologies of both parents and patient were

negative. As in this instance, an attack characteristically follows exposure to cold or may be brought on by immersing the hands in cold water. The patient complains of subjective chilly sensations, which are followed by shaking chills, fever, abdominal pain, blanching of the extremities and occasionally urticaria. Within an hour thereafter, reddish brown urine is voided. These attacks last from two to four hours and the urine clears within twenty-four to forty-eight hours. According to the severity and the frequency of attacks, jaundice and a secondary anemia may develop.

It has been demonstrated by the Donath-Landsteiner test that there is an auto-iso-hemolysin in the blood of these patients which acts on red cells heated to room temperature after exposure to cold. When serum of the patient mixed with an equal volume of cells, either of the patient or of the same blood group, is exposed to a temperature of 4° to 8° centigrade for 10 minutes, and then placed in an incubator at 37° centigrade for 30 minutes, hemolysis takes place. The theory suggested to explain the disease process is that the auto-hemolysins combine with the erythrocytes in the cooled portion of the body and when these cells are subsequently warmed, complement, which is present normally in blood plasma, completes the reaction and hemolysis occurs.

Cold agglutinins are also demonstrable in this disease and were present in the blood of this child. When serum containing non-specific cold agglutinins is mixed with human red cells at 0 and 5° centigrade, agglutinations of the red cells takes place. The titre of these agglutinins is increased in certain diseases so that agglutination may take place at room temperature; these diseases include paroxysmal hemoglobinuria, syphilitic or hypertrophic cirrhosis of the liver, hemolytic icterus, Raynoud's disease, trypanosomiasis, severe anemias and virus pneumonias. This phenomenon might account for the severe transfusion reaction the child experienced when warm fresh blood was used.

Other rarer types of paroxysmal hemoglobinuria not appearing after exposure to colds include: (1) nocturnal paroxysmal hemoglobinuria, in which the red cells are sensitive to an increased carbon dioxide content of the blood, (2) march hemoglobinuria, which occurs after severe muscular exercise, and (3) paralytic hemoglobinuria, which is accompanied by muscular weaknesses and cramps and is attributed to a sensitivity of the red cells to lactic acid.

CLINICO-PATHOLOGICAL CONFERENCE

Directed by — Dr. E. Clarence Rice

Assisted by — Dr. John E. Cassidy

Held every Tuesday afternoon at 3:00 p. m.

MESENTERIC CYST

Case No. 18

Dr. John Cassidy L.L. 33-3626

L. L., a two and one half year old male, was admitted to Children's Hospital on June 15, 1933 because of the presence of an abdominal mass.

This mass was first noted by the mother approximately one year previously. About six months later, the right upper portion of the abdomen began to enlarge and later on, it was noted that there were two masses present, this being confirmed in another hospital.

The child's general health had been excellent. His appetite was always good, his bowels regular. There was no urinary complaint. At no time was there any apparent abdominal pain.

Physical examination showed a well developed, well nourished child with a protuberant abdomen. The positive physical findings were confined to the abdomen which showed two rounded tumors, a smaller one in the right upper quadrant and a larger one in the lower left quadrant. The upper tumor moved with respiration and extended from the mid-line well into the right flank, down almost to the umbilicus and up beneath the right costal margin. It was rounded, smooth, fluctuant, non-tender, slightly moveable from side to side and there was a distinct elongated lobule which extended into the right flank. The whole tumor mass seemed to be just beneath the anterior abdominal wall and its upper margin could not be distinctly separated from the liver. There was percussion dullness over this mass.

The lower tumor had the same physical characteristics as the other. It extended well into the left flank and 1½ to 2 inches to the right of the mid-line. The lower margin was below the anterior superior iliac spine but did not extend into the pelvis; the upper margin was 2 inches below the left costal margin. It was freely movable and could be pushed over to the right side of the abdomen and up to the costal margin. There was a sulcus between the two masses and it was believed that a communication existed between the two since firm pressure on one would cause an increased tension in the other. The edge of the spleen was palpated just beneath the left costal margin and was separate from

the tumor. The kidneys were not palpable. The remainder of the physical examination was essentially negative.

Roentgenological studies revealed the masses to be outside of the gastro-intestinal tract.

Aspiration of the tumors was performed and examination of the fluid revealed the presence of amylase and trypsin. A communication between the two masses was demonstrated by the injection of methylene blue into one and recovering it in the other.

Blood studies and urinalyses were negative.

Two days after entry, laparotomy was performed, the pre-operative diagnosis being multiple abdominal cysts, probably mesenteric or pancreatic in origin.

At operation, a smooth cystic tumor, the size of a large grapefruit was found in the lower left quarant, and its upper end was an isthmus 1½ inches long which connected it with a smaller, cystic rounded, smooth tumor the size of a small grapefruit in the right upper quadrant. To the right of the upper tumor was a sausage like prolongation about 2 inches in diameter that extended to the right flank and then backward, upward, and medially behind the stomach to the pancreas. The latter appeared normal. The two large, rounded cysts were incorporated in the gastrocolic omentum, the mesentery of the entire descending colon, and partly in the mesentery of the ileum. They were dissected free of the mesentery and removed. The sausage like portion was then explored. It was thick walled and its lining resembled intestinal mucous membrane, being thrown into circular folds. It was opened and dissected free. At its end, there was a small fistula which on probing ran upward for a distance of 2½ to 3 inches apparently in the substance of the pancreas. The fistula was closed and the end sutured to the peritoneum at the upper end of the incision, after removing the sausage shaped tumor.

Microscopic sections of the cysts showed two layers of smooth muscle on which was superimposed a layer of mucous membrane of practically uniform thickness, in general resembling the structure of intestinal mucosa.

The immediate post-operative condition was good. The incision healed per primum except for the opening of the fistula at the upper end of the incision. This continued to discharge a small amount of serum which was unlike the fluid found in the cyst.

The patient was discharged from the hospital on the 28th post-operative day in good condition and with a marked decrease in the amount of drainage from the fistula.

DISCUSSION

Dr. J. Ogle Warfield: * Mesenteric tumors are rare, the cystic variety being more common than the solid neoplasm. Mesenteric cysts have been observed since early in the 16th century, though successfully operated only in the past 65 years.

Their origin is (1) embryonic remnants of retroperitoneal organs such as germinal epithelium, ovary, Wolffian or Mullerian bodies which have become displaced forward between the layers of the mesentery or (2) displaced embryonal sequestrations from intestinal diverticula or the vitelline duct.

These tumors occur more frequently in the small than the large bowel, and more commonly in the ileum than elsewhere along the gastro-intestinal tract. They may be single or multiple, large or small, unilocular or multilocular. The structure of the cyst wall may reveal the genesis of the tumor, while the contents often denote accidents that have befallen the cyst and seldom have any bearing on its etiology.

The presenting signs are those of a silent, cystic, movable abdominal tumor, often strikingly movable in the transverse direction due to its mesenteric attachment. It must be differentiated from retroperitoneal cysts, cysts of the kidney, pancreas, ovary, liver and spleen, and hydrops of the gall bladder. When large, it may be confused with ascites and tuberculous peritonitis. The diagnosis is often obscured by complications, the most frequent being intestinal obstruction of a mechanical nature. Other complications may include hemorrhage into the cyst, rupture, torsion, impaction into the pelvis, and peritonitis which may follow obstruction. In the presence of complications, the condition may simulate other causes of an acute surgical abdomen.

The treatment of mesenteric cysts may have to be directed principally toward the complications. Otherwise it consists of (1) enucleation, the operation of choice when possible; (2) enucleation with intestinal resection; (3) either marsupialization or drainage. Aspiration may be helpful diagnostically but should not be employed as a method of treatment. Diagnostic puncture is not always wise, but if resorted to, one should be reasonably sure that intestines are not interposed between the cyst and abdominal wall. Operative intervention should be planned to follow soon thereafter because of possible leakage of the cyst contents into the peritoneal cavity. The cyst contents may be clear, colorless, yellow, milky, mucinous, brown, sebaceous, or bloody. The reaction is alkaline and the specific gravity about 1.015 or 1.016. It often contains a large amount of albumin, cell debris, blood and cholestrin.

* Member of the Attending Surgical Staff, Children's Hospital, Washington, D. C.

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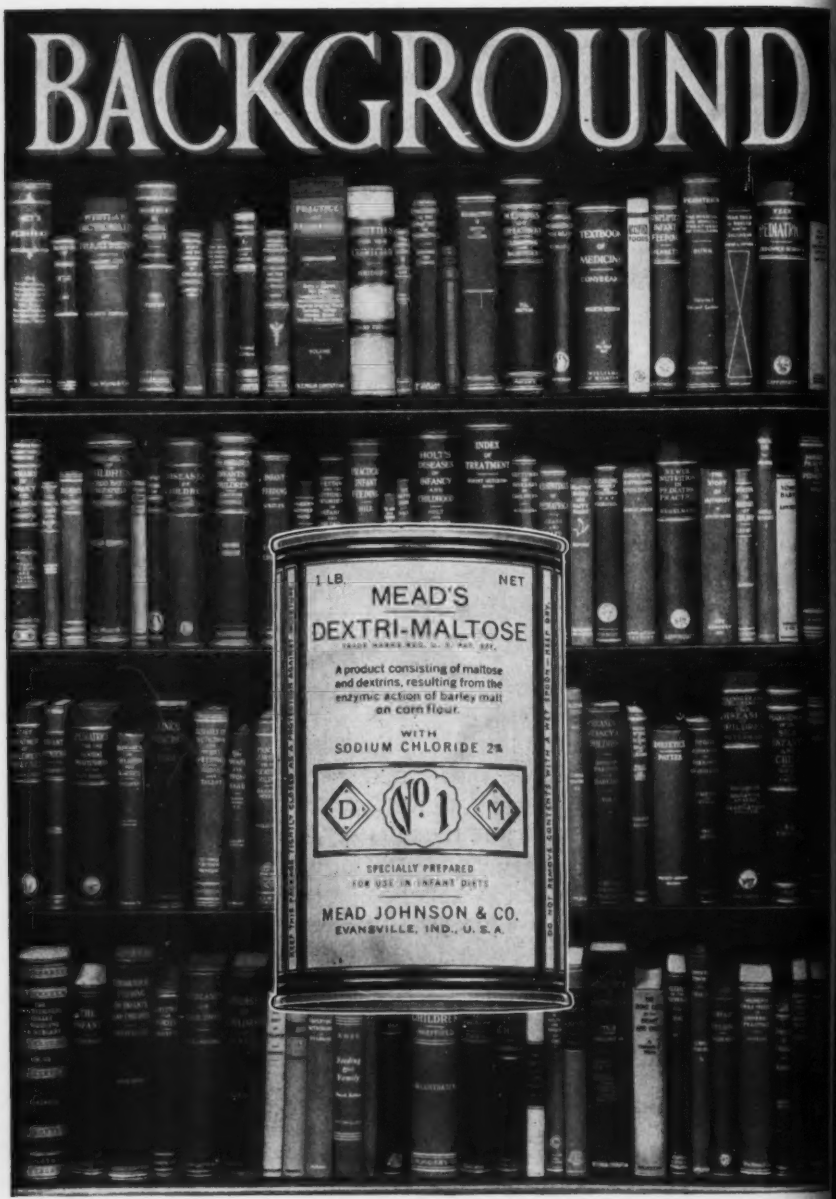
BACKGROUND



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